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A CASE OF METASTATIC CARCINOMA OF THE SPINE AND MENINGES.

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The case reported in this paper is of interest not only because it is one of a class of diseases which rarely occurs, but also for the reason that some of the symptoms usually associated with cancer of the spine were not present.

I am indebted to Dr. Charles W. Burr for the privilege of studying the case clinically, and for the opportunity of studying the pathological material obtained at the necropsy.

K. B., female; aged 63; nativity France, was admitted to the Philadelphia Hospital February 12, 1901. The family history was negative. The patient had been in good health until six years previous to her admission to the hospital, when she had an attack of what she called "rheumatism." During the same year she injured her left breast, to what extent is unknown.

One year before she entered the hospital she had an attack of violent pain in the back. This lasted but a day, and she was able to be out of bed the following day, though she had some difficulty in walking. This difficulty steadily increased, and for three months previous to admission to the hospital she had been confined to her bed.

She complained of pain in the left shoulder, inability to control her bladder, that is, the urine dribbled, and there was obstinate constipation. No other definite subjective symptoms could be obtained.

Physical Examination.—The patient was confined to bed because of inability to move her legs. There was no palsy of the face; the tongue protruded straight; there was no palsy in either arm, but both hands were weak and when extended there was a tremor in both. There was a slight bowing of the spine in the superior thoracic region—that is—the patient was "stoop-shouldered," but there was no angular deformity.

Both legs were completely paralyzed and there was bilateral "foot-drop." The legs were edematous, particularly the right. There was wasting of the thighs and calves, particularly the left thigh. Muscle reactions were not taken. As to the reflexes both biceps-jerks were slightly increased. The knee-jerks were absent. The Achilles-jerk was present on the left but absent on the right. Stroking the sole of the left foot caused extension of all the toes except the little toe, and this was very marked. On the right side there was very slight extension of the great toe.

Sensation to touch was normal on the face, hands and arms. In the legs it was preserved, but the patient could not localize.

The blood-count showed a great diminution of the red cells, 2,250,000; and an increase in the leucocytes, 13,500.

There was a large ulcerating bed-sore over the sacrum, another on the hip, and a third (a small one) over the right superior iliac spine. The left breast was the seat of a hard nodular growth.

The patient's condition grew rapidly worse, the bed-sores becoming larger, and wherever there was pressure others appeared. On the seventh day after admission the temperature became subnormal and remained between 94 and 95, until her death, which occurred on the eleventh day.

The necropsy, made by Dr. W. F. Hendrickson, revealed the following: the left breast showed an indurated mass, the cut surface was mottled grayish-yellow, and showed many interlacing white bands. There was no ulceration, nor were the axillary lymph glands enlarged. There was edema and hypostatic congestion of the lungs, the liver was large and fatty, and the spleen contained several infarcts. The kidneys were of the small granular variety, and the aorta was considerably thickened, being calcified in patches. There were no metastases in any of the viscera.

At the level of the fourth dorsal vertebra and extending downward about five centimeters, the dura was adherent to the adjacent bone. On separation, the surface of the greatly thickened dura was seen to be covered with grayish-pink granulations. There was no apparent involvement of the pia or arachnoid. At this same level, there was a slight kyphosis, and the bone was distinctly softened, cutting like cartilage, but there was no tumor of the bone.

For histological examination, pieces of the diseased bone and the first four cervical segments of the spinal cord were hardened in formalin. The remainder of the cord was hardened in Müller's fluid. Sections of the bone were stained with hemalum and eosin; the cord sections were stained with the Weigert method, hemalum-eosin, hematoxylin-eosin, and sodium carminate. The primary growth was sectioned and stained by Dr. Hendrickson, to whom I am indebted for slides of the same, which show all the characteristics of scirrhus carcinoma. Sections made from the affected vertebræ show very little bone substance, nevertheless, between the trabeculæ-like masses of osteoid tissue may be seen nests of cells similar to those in the primary growth. Some of the trabeculæ are cartilaginous in appearance. In the areas where there is not an invasion by the cancer cells, there is an infiltration of round and spindle-shaped cells, together with leucocytes. The periosteum is thickened and infiltrated though not with cancer cells.

Grossly, the cord showed a thickening of its dura extending from the fourth to the ninth dorsal segments. After hardening there could be seen extending throughout the cervical, and in the dorsal region as far as the seventh segment, a light-colored area corresponding to the postero-median columns. In the seventh segment no such localized area could be discerned, except in the lower part, where the crossed pyramidal tracts were seen to be affected, extending as far as the lumbar part of the cord. Sections were made from each segment, beginning with the first cervical and ending with the conus.

In the cervical segments, sections stained with nuclear stains show the pia to be infiltrated with small round cells, which infiltration follows the path of the blood-vessels. The veins show a marked infiltration of the connective tissue surrounding them. The white matter shows an increase in the neuroglia, particularly in the posterior and lateral parts of the cord, as is evidenced by the large number of nuclei of glia cells. Here and there can be seen vacuoles replacing the nerve fibers. The gray matter shows its substance to be very vascular, the ganglion cells being for the most part normal. The central canal is patulous and the cylindrical epithelium easily distinguished.

In the Weigert-stained preparations, an area of apparent degeneration appears in the column of Goll of each half of the cord. This area extends but two-thirds of the distance from the periphery to the gray commissure. When examined under high power the apparently degenerated (that is, the faintly-stained areas) show an increase of the neuroglia, rather than an actual degenerative process, inasmuch as there are many well-staining nerve fibers distinctly separated from each other by neuroglia. In the fifth segment the direct cerebellar tract shows a distinct neurogliar increase.

The dorsal part of the cord shows the greatest amount of change. The upper segments are in some respects similar to those of the cervical part of the cord. The dura is thickened, more posteriorly than anteriorly; the pia is also somewhat thickened, its vessels distended with blood and their walls infiltrated with small round cells, particularly beneath the intima. The entire cross section gives the appearance of a distinct neurogliar overgrowth, most marked as before mentioned, in the posterior columns (Goll). In Weigert-stained preparations these columns are but faintly stained, and in the vicinity of Gowers' bundle in the left half of the cord there is a marked increase of neuroglia. In the part of the white matter where the neuroglia is not so marked the axis-cylinders are swollen. The ganglion cells seem not to be changed except that their protoplasm is slightly granular. As the sections descend the thickening of the membranes becomes more marked and the interstitial overgrowth increases in the white matter. The cellular infiltration becomes more marked and seems to have invaded the nerve roots. Upon examining the upper part of the third dorsal segment, the outer surface of the dura on the anterior aspect of the cord shows a small amount of loose connective tissue adhering to it, and in the lymph spaces are seen several nests of large, deeply-stained nuclei, most of which are larger than a mononuclear leucocyte, and are apparently identical with the cells of the primary growth in the breast and those in the vertebræ. The nerve roots do not contain any of the cells just described. The fourth, fifth and sixth segments show a very much thickened dura and a much greater number of nests of large cells. In sections from the fifth segment one of the nerve roots contains a single cluster of cells similar to those found in the dura.

The sixth dorsal has the greatest amount of thickening of the dura and of infiltration with cancer cells. No cancer infiltration is seen in the pia. In sections stained by the Weigert method, the replacement of the nerve fibers by neuroglia is shown to be in patches both in the posterior and lateral columns. The gray matter contains an overgrowth of neuroglia and is not easily distinguished from the white matter, containing, however, numerous apparently normal ganglion cells.

At the level of the seventh dorsal segment the destruction is most marked. The growth of neuroglia far exceeds that found in the other segments, and is most marked posterior to the gray commissure and in the lateral columns of the right half of the cord, where the nerve fibers are practically absent. Sections made in the upper part of the segments contain more normal fibers than the deeper ones. In the lower third of the segment (approximately) the interstitial tissue is more diffusely arranged, except in the crossed pyramidal tracts, where there are no normal fibers to be seen. The central canal is patulous in the upper part of the segment, but where the greatest amount of connective tissue is found the canal is filled with deeply staining round cells. The gray matter is shrunken and distorted, no ganglion cells can be found. The vessels in the nerve roots stain very faintly, though the cells of the intima are apparently normal. The vessels in the meninges stain deeply.

Below the seventh segment the meningitis is less marked. There are a few cancer cells to be seen scattered irregularly through the various segments. Some sections, however, show none. The proliferation of neuroglia is less marked than above, as is the degeneration in the crossed pyramidal tracts. Where there is an actual degeneration it occurs in scattered patches in the crossed pyramidal tracts. In the eighth segment the artery of the anterior fissure is very much thickened, the intima in particular. This is more marked than at any other level. The tenth segment shows more of the carcinoma infiltration than any of the segments below the seventh, and is much less than that described above. The cells of the anterior horns are very much shrunken—nuclei in many instances cannot be seen, and in others, the nuclei are pushed to the extreme edge of the cells.

The lumbar segments do not show marked changes in the white substance. There is an increase in the neuroglia, particularly in the crossed pyramidal tracts, and a few scattered patches of degeneration. There is a mild grade of meningitis; the nerve fibers in the roots stain very well by the Weigert method—better in the anterior roots than in the posterior, though hematoxylin-eosin stained preparations show an increase in the number of small round cells among the nerve fibers.

That carcinoma of the spine is a rare disease is shown by the work of Schlesinger, who, after examining the reports of the Vienna Pathological Institute, found that in 3,720 cases of carcinoma there were 54 with metastasis in the vertebræ and meninges of the spinal cord. In addition, he speaks of five cases observed personally. This report together with the very complete bibliography which accompanies it, has been valuable to me in studying the subject.

It is held by some that cancer of the spine may occur primarily, but the bulk of evidence seems to prove that it either occurs as a secondary growth, or from contiguous structures. When the growths in the spine are metastatic, as they are in most instances, they most frequently follow carcinoma of the breast, as is shown by the following table (Schlesinger's):

Breast	in	10	cases.
Esophagus	"	9	"
Thyroid	"	9	"
Uterus	"	6	"
Bronchus	"	5	"
Stomach	"	4	"
Prostate	"	3	"
Gall bladder	"	2	"
Ovary	"	1	"
Sigmoid flexure	"	1	"
Rectum	"	1	"
Kidney	"	1	"
Adrenal	"	1	"
Pancreas	"	1	"
Not specified	"	1	"

Bruns reports five cases occurring after breast disease. Osler describes four cases, one of which gave symptoms of increased reflexes and nerve-root pain only. In none of his cases was there an autopsy. Boettiger reported a case in which, after removal of a mammary growth, there were spinal symptoms and the findings of cancerous infiltration into the vertebræ. Amidon reports three cases and reviews the literature, concerning thirteen cases.

Two cases are reported by Scanzoni—one, in which the growth, secondary to cancer of the breast, invaded not only the vertebræ and meninges, but also gained entrance to the substance of the cord at the point of entrance of the posterior roots. The second case, after carcinoma of the thyroid, showed the substance of the cord to be involved, the process having followed the line of the anterior root and the posterior median fissure. Terrier describes a case in which the lower three lumbar vertebræ and part of the sacrum were affected secondarily to cancer of the breast. There was no involvement of the cord or nerves. Concerning metastasis in the spine after carcinoma of other organs, several reports occur in the literature. Simon mentions two cases—one, after cancer of the kidney with involvement of two lumbar vertebræ; another, following cancer of the esophagus with involvement of the cervical vertebræ. Nonne reported a case following cancer of the stomach.

Like other forms of spinal disease, carcinoma produces symptoms referable to the bone, the nerve-root and spinal cord.

Of the bone symptoms deformity is the most important. It is not always present, and when observed it is usually less marked than that in tuberculous spinal disease. According to Amidon's table, the deformity exists most frequently in the dorso-lumbar region. Bone pain is not a constant symptom and when it is present, the diseased vertebræ, in many instances, are not sensitive to pressure. Rigidity of the spine is usually present.

Of the nerve-root symptoms, those sensory are usually the first noticed. Pain is the most important, and usually continues throughout the course of the disease, though some cases do run their course without severe pain. The pain associated with the motor symptoms led Cruveilhier to term it "paraplegia dolorosa," which condition Charcot later associated with cancer. The important feature concerning the pain is that it is radiating in character, and made worse by movement. Anesthesia is said not to be frequent, but hyperesthesia and paresthesia are common symptoms. Herpes zoster occurs in many instances.

Of the motor symptoms, the palsy, though not the first symptom, may come on suddenly. Schlesinger cites a case in which it came during the night—no lesion of the cord substance having been found, but the nerve roots were distinctly damaged. He also mentions the fact that where the nerve roots alone are affected, fibrillary twitchings are apt to precede the palsy, and atrophy rapidly follows.

The symptoms referable to cord involvement may be slow in onset, the result of an advancing compression myelitis; or, sudden, through the displacement of the vertebræ, and, followed by the symptoms of vertebral caries. The resulting palsy will depend upon the level of the cord affected. In other instances the onset is similar to that of a transverse myelitis with palsy of the extremities below the lesion, loss of control of the bladder and rectum, loss of sensibility, skin and tendon reflexes, followed by atrophy and trophic ulceration.

The case just related gave an indefinite history of pain, called "rheumatism," several years before there was any difficulty in muscular activity. Whether this is one of the cases, as are described by Charcot, in which the cancer remains latent in the vertebræ and suddenly becomes active, is impossible to say, as the personal history furnishes no definite guide. The pain, in all probability, was not a nerve-root pain, since other symptoms, which would have been associated with it, were not present. During the height of the disease there was little pain. There was no visible deformity of the spine. There was a flaccid palsy of both legs; bladder and rectal control were lost; with the exception of one Achilles jerk and the Babinski reflex on each side—more on one than the other—the reflexes were lost.

From the foregoing facts it may be concluded that the pain, which together with the other sensory symptoms, may exist for a long time without any palsy, is due, not to the bone disease, but is the sign of nerve-root involvement. On the other hand, when absent, palsy and other cord-symptoms being present, it is to be inferred that the cord-disease has been so rapid as to exclude the transmission of sensory influences, in which instances there will also be anesthesia; or, that the nerve roots are not at all affected. Secondly, that the palsy may be due either to pure root involvement, or to disease of the substance of the cord—a compression myelitis. Thirdly, that vertebral carcinoma may run its course without severe pains, therefore, not always producing the "paraplegia dolorosa."

The absence of severe pains with the presence of nerve-root involvement at levels of the cord higher than that at which there was a great destruction of its substance, can only be explained by the personal equation, since we know of the presence or absence of pain by the word of the patient. The absence of anesthesia in this case makes it impossible to account for the absence of pain in any other way. The absence of marked deformity simply means that the secondary process in the cord (the interstitial overgrowth) following the meningitis progressed more rapidly than the neoplasm in the vertebræ.

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